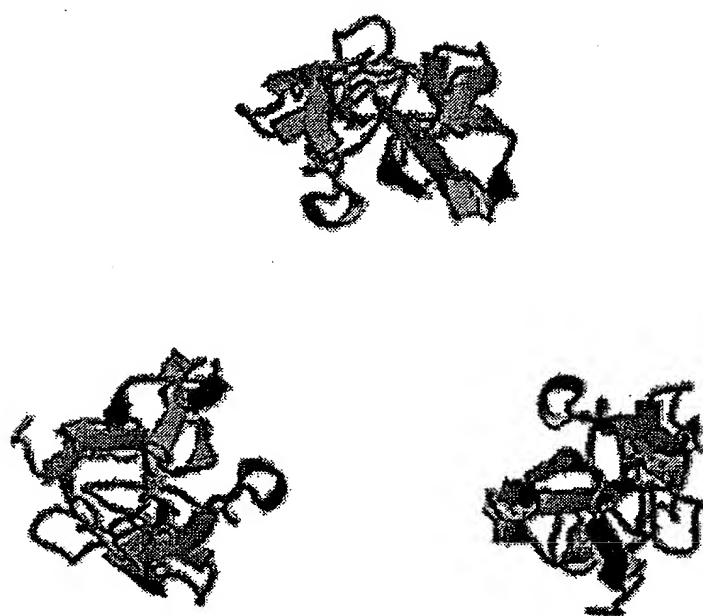


**FIGURE 1**

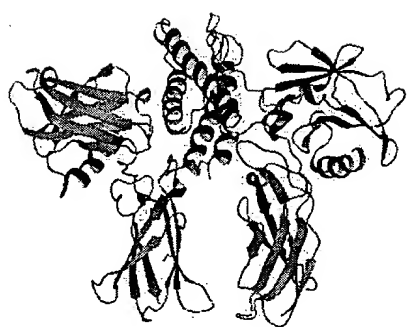






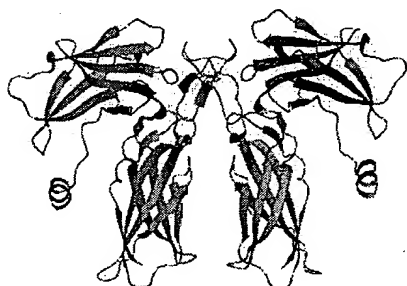
TNFR trimer

**FIGURE 4**

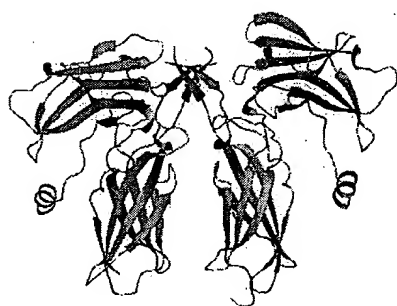


EPO-(EPOR)<sub>2</sub>  
Natural protein

Potent agonist

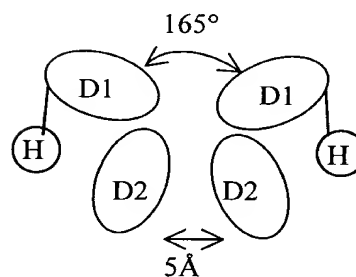
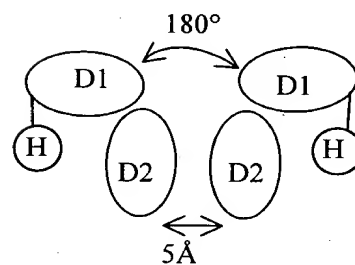
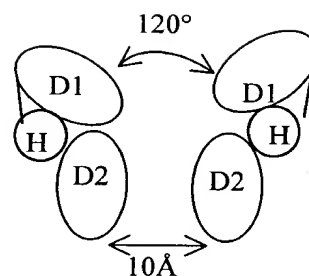


(EMP1-EPOR)<sub>2</sub>  
Weak agonist



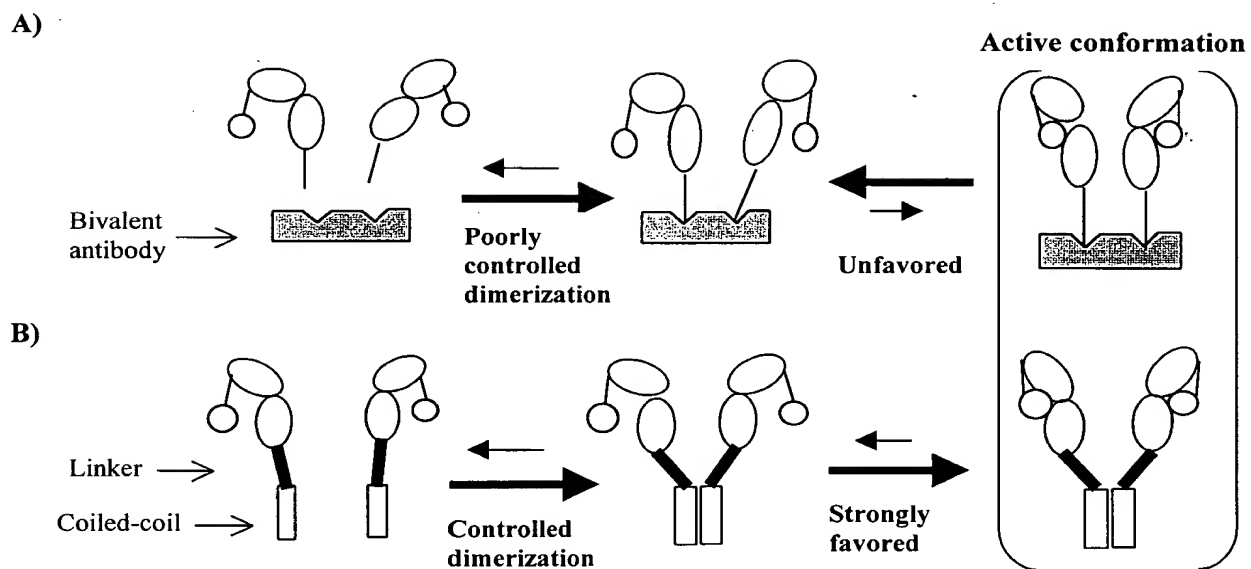
(EMP33-EPOR)<sub>2</sub>  
Antagonist

EPOR complexes with ligands

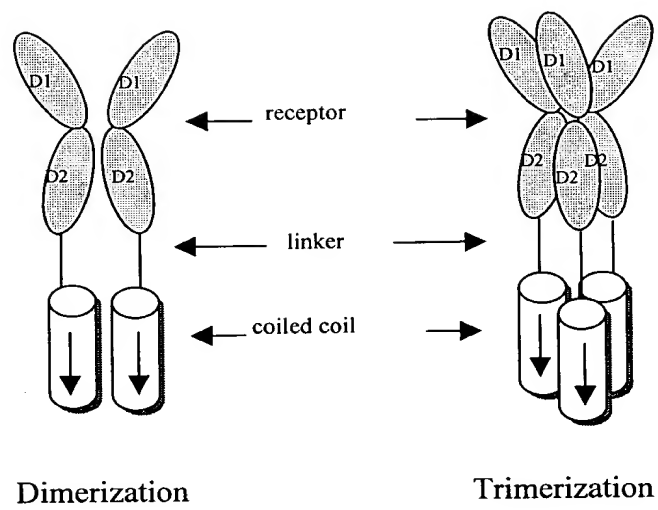


EPOR complexes without ligands

**FIGURE 5**



**FIGURE 6**



**FIGURE 7**

Query: 1 APPPNLPDP 9

10 20 30 40 50 60  
Query: 10 KFESKAALLAARGPEELLCTERLEDLVCFWEEAASAGVGPGNYSFSYQLEDEPWKLCRL 69

Subject: 1 KFESKAALLAARGPEELLCTERLEDLVCFWEEAASAGVGPGNYSFSYQLEDEPWKLCRL 60

| PDA sites   | * | * | * | * |
|-------------|---|---|---|---|
| lebp_d1_e2  |   | F | F |   |
| lebp_d1     | F | F | F |   |
| lebp_d2     |   |   |   |   |
| lebp_d12    | F | F | F |   |
| leer_d1     |   | F | F |   |
| leer_d1_211 |   | F | I | I |
| leer_d1_422 | F | F | F |   |
| leer_d2     |   |   |   |   |
| leer_d2_211 |   |   |   |   |
| leer_d2_422 |   |   |   |   |
| lblw_d1     |   | F | F |   |
| lblw_d1_211 |   | F | F |   |
| lblw_d1_422 |   | F | F |   |
| lblw_d2     |   |   |   |   |
| lblw_d2_211 |   |   |   |   |
| lblw_d2_422 |   |   |   |   |

| elbow_PDA   | * | * | *** | * | * | * |
|-------------|---|---|-----|---|---|---|
| leer_ew     |   | F |     |   |   |   |
| leer_ew1    |   | L |     | L | I |   |
| leer_ew2    |   | F | W   |   |   |   |
| lblw_ew     | L | Y | V   |   | I |   |
| lblw_ew1    | W | L | I   | L | L |   |
| lblw_ew2    | L | W | Y   |   | I |   |
| lebp_ew     | Y | L | YW  | Y | I |   |
| lebp_ew1    | A | Y | Y   | Y | I | Y |
| lebp_ew2    | Y | L | IYW | Y | I | Y |
| leer_17_ew1 | K | M | M   |   | E |   |
| leer_17_ew2 |   | S | K   | W | Q |   |
| lebp_17_ew1 | Q | R | ND  | R | E | Y |

FIGURE 8A



70                      80                      90                      100                      110                      120  
 Query: 70 HQAPTARGAVRFWCSLPTADTSSFVPLELRVTAASGAPRYHRVIHINEVVLLDAPVGLVA 129  
 Subject: 61 HQAPTARGAVRFWCSLPTADTSSFVPLELRVTAASGAPRYHRVIHINEVVLLDAPVGLVA 120

| PDA sites   | * | * | * | * | * | * | *  | *   |
|-------------|---|---|---|---|---|---|----|-----|
| lebp_d1_e2  | I |   |   |   |   | F |    |     |
| lebp_d1     | I |   |   | L |   | F |    |     |
| lebp_d2     |   |   |   |   |   |   |    |     |
| lebp_d12    | I |   |   | L |   | F |    |     |
| leer_d1     | I |   |   |   |   | F |    |     |
| leer_d1_211 | Y |   |   | F |   | F |    |     |
| leer_d1_422 | I |   |   | L |   |   |    |     |
| leer_d2     |   |   |   |   |   |   |    |     |
| leer_d2_211 |   |   |   |   |   |   |    |     |
| leer_d2_422 |   |   |   |   |   |   |    |     |
| lblw_d1     | I |   |   | L |   | F |    |     |
| lblw_d1_211 | I |   |   | L |   | F |    |     |
| lblw_d1_422 | I |   |   | L |   | F |    |     |
| lblw_d2     |   |   |   |   |   |   |    | I V |
| lblw_d2_211 |   |   |   |   |   |   |    |     |
| lblw_d2_422 |   |   |   |   |   |   |    | I   |
|             |   |   |   |   |   |   |    |     |
| elbow_PDA   |   |   |   |   |   |   | ** |     |
| leer_ew     |   |   |   |   |   |   |    |     |
| leer_ew1    |   |   |   |   |   |   |    |     |
| leer_ew2    |   |   |   |   |   |   |    |     |
| lblw_ew     |   |   |   |   |   |   |    |     |
| lblw_ew1    |   |   |   |   |   | F |    |     |
| lblw_ew2    |   |   |   |   |   |   |    |     |
| lebp_ew     |   |   |   |   |   |   | W  |     |
| lebp_ew1    |   |   |   |   |   |   | Y  |     |
| lebp_ew2    |   |   |   |   |   |   | W  |     |
| leer_17_ew1 |   |   |   |   |   |   |    |     |
| leer_17_ew2 |   |   |   |   |   |   |    |     |
| lebp_17_ew1 |   |   |   |   |   |   | EM |     |

FIGURE 8B

130            140            150            160            170            180  
 Query: 130 RLADESGHVLRWLPPTTPMTSHIRYEVDVSAGNGAGSVQRVEILEGRTECVLSNLRGR 189  
 Subject: 121 RLADESGHVLRWLPPTTPMTSHIRYEVDVSAGNGAGSVQRVEILEGRTECVLSNLRGR 180

| PDA sites   | * * * | * * * | * | * |
|-------------|-------|-------|---|---|
| lebp_d1_e2  |       |       |   |   |
| lebp_d1     |       |       |   |   |
| lebp_d2     | I     | F L I | L |   |
| lebp_d12    | I     | F L I | L |   |
| leer_d1     |       |       |   |   |
| leer_d1_211 |       |       |   |   |
| leer_d1_422 |       |       |   |   |
| leer_d2     |       | W I I |   |   |
| leer_d2_211 |       | F I I |   |   |
| leer_d2_422 |       | W L I |   |   |
| lblw_d1     |       |       |   |   |
| lblw_d1_211 |       |       |   |   |
| lblw_d1_422 |       |       |   |   |
| lblw_d2     | I I   | F I I |   |   |
| lblw_d2_211 |       |       |   |   |
| lblw_d2_422 | I I   | F I I |   |   |

**elbow\_PDA**

leer\_ew  
 leer\_ew1  
 leer\_ew2  
 lblw\_ew  
 lblw\_ew1  
 lblw\_ew2  
 lebp\_ew  
 lebp\_ew1  
 lebp\_ew2  
 leer\_17\_ew1  
 leer\_17\_ew2  
 lebp\_17\_ew1

**FIGURE 8C**

190                      200                      210                      220  
 Query: 190 TRYTFAVRRARMAEPSFGGFWSAWSEPVSLLT 220 PSDLD 225

Subject: 181 TRYTFAVRRARMAEPSFGGFWSAWSEPVSLLT 211

| PDA sites   | * * * * | * | * |
|-------------|---------|---|---|
| lebp_d1_e2  |         |   |   |
| lebp_d1     |         |   |   |
| lebp_d2     | I I     |   |   |
| lebp_d12    | I I     |   |   |
| leer_d1     |         |   |   |
| leer_d1_211 |         |   |   |
| leer_d1_422 |         |   |   |
| leer_d2     | F V     |   | F |
| leer_d2_211 | V       |   | F |
| leer_d2_422 | F       |   | I |
| lblw_d1     |         |   |   |
| lblw_d1_211 |         |   |   |
| lblw_d1_422 |         |   |   |
| lblw_d2     | I I I   |   | I |
| lblw_d2_211 |         |   |   |
| lblw_d2_422 | I L I   |   |   |

| elbow_PDA   | ** | * |
|-------------|----|---|
| leer_ew     | W  |   |
| leer_ew1    |    | Y |
| leer_ew2    | WF |   |
| lblw_ew     | WI |   |
| lblw_ew1    | IY |   |
| lblw_ew2    | WI |   |
| lebp_ew     | W  |   |
| lebp_ew1    | W  |   |
| lebp_ew2    | W  |   |
| leer_17_ew1 | ME | Y |
| leer_17_ew2 | WE |   |
| lebp_17_ew1 | N  |   |

**FIGURE 8D**